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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ASHEN, JON BENJAMIN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/820,060	DESGROSEILLERS ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-30 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-30 are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Revised Notice to Comply*.

DETAILED ACTION

Objections to the Specification

Sequence Compliance

1. The disclosure is objected to because of the following: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. In the instant case, figure 12 depicts nucleotide sequences that are greater than 10 residues that are not accompanied, either on the figure, or in the Brief Description text, with the required SEQ ID NO:.

The above listing of figure 12, which sets forth nucleotide sequences that require SEQ ID NO: is by way of illustration. In order to be fully responsive to this Office Action, Applicant should review this application in its entirety to ensure compliance with the requirements of 37 CFR 1.821 through 1.825 and to make all appropriate corrections.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-17, 21, 23 (in part), 24 and 30, drawn to a siRNA that downregulates expression of a Staufen gene comprising a sense region that is at least 95% identical to a portion of a Staufen nucleic acid selected from the group consisting of SEQ ID NO: 1, 3, 5, 6 and 7,

classified in class 536, subclass 24.5 (This group is further restricted below).

II. Claims 18-20, 22, drawn to a method for inducing RNA interference in a subject or of treating or preventing a RNA virus infection in a subject comprising administering a pharmaceutical composition comprising an siRNA that reduces Staufen protein expression, classified in class 514, subclass 44 (This group is further restricted below).

III. Claim 23 (in part), drawn to an antisense oligonucleotide comprising at least 10 contiguous nucleotides at least 95% complementary to any one of SEQ ID NO: 1, 3, 5, 6, 7 and 10, classifiable in class 536, subclass 24.5 (This group is further restricted below).

28+29

IV. Claims 23 (in part), drawn to a pharmaceutical composition or vaccine comprising a mammalian Staufen protein or portion thereof selected from the group consisting of SEQ ID NO: 1, 3, 5, 6 and 7, classifiable in class 530, subclass 350+ (This group is further restricted below).

V. Claims 25-27, 28 (in part) and 29, drawn to a chimeric protein comprising a first and second portion wherein the first portion encodes a Staufen protein or portion thereof selected from the group consisting of SEQ ID

NO: 2, 4, 8 and 10, classifiable in class 530, subclass 350+ (This group is further restricted below).

VI. Claims 23 (in part), 28 (in part) and 29, drawn to a pharmaceutical composition or vaccine comprising a nucleic acid encoding a Staufen protein or fragment thereof selected from the group consisting of SEQ ID NO: 2, 4, 8 and 10 (This group is further restricted below).

3. The inventions are distinct, each from the other because of the following reasons:

4. Inventions of groups I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). The inventions in group I are drawn to an siRNA that downregulates expression of a Staufen gene comprising a sense region that is at least 95% identical to a portion of a Staufen nucleic acid selected from the group consisting of SEQ ID NO: 1, 3, 5, 6 and 7. The invention of group II is a method for inducing RNA interference in a subject or of treating or preventing a RNA virus infection in a subject comprising administering a pharmaceutical composition comprising an siRNA that reduces Staufen protein expression. In the instant case the product as claimed can be used in a materially different process of using that product which would be an in vitro method of characterizing gene and protein function.

Furthermore, searching any of the Inventions in group I with the invention of group II would impose a serious and undue burden. In the instant case, prior art searches of the composition and the methods of administering the claimed composition would not be coextensive. Search of each of these inventions would require different key word searches and would include, at least, a search for particular sequences required by the compositions that are not required by the method and for the distinctive steps required by the method that would not be required by the composition. These searches would need to be performed in divergent patent, sequence and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious and undue burden on the Office in terms of both search and examination. As such, it would be burdensome to perform a search and examination of any of the inventions in groups I and the invention of group II together.

5. Inventions I and III-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn compositions that require to structurally and chemically distinct molecules that are the siRNAs of group I, the antisense oligonucleotide of group III, the proteins of group IV, the chimeric proteins of group V or the nucleic acids of group VI. Moreover, each of the inventions of groups I and II-VI has a different mode of operation. Each is claimed as a pharmaceutical or

vaccine and each, therefore, operates to provide a treatment effect based on the structure and chemistry of the required siRNA, antisense oligonucleotide, protein, chimeric protein or nucleic acid that encodes a protein, respectively. siRNA operates by mediating RNA interference. Antisense oligonucleotides can operate by an RNase H dependent mechanism that siRNAs cannot operate by. Proteins operate by binding mechanisms related to their primary amino acid structure, which are distinguished from both siRNAs and antisense oligonucleotide which can operate by Watson-Crick hydrogen bonding between complementary nucleobase pairs. Chimeric proteins operate by binding mechanisms related to their primary amino acid structure and are distinguished from non-chimeric proteins by function related to that particular and unshared structure; the mammalian Staufen proteins or portions thereof selected from the group consisting of SEQ ID NO: 1, 3, 5, 6 and 7 that are the inventions of group IV are apparently different than the inventions of group V, which are claimed as Staufen proteins or portions thereof selected from the group consisting of SEQ ID NO: 2, 4, 8 and 10. Nucleic acids encoding proteins operate by a gene therapy mechanism to provide a transcriptional template for a particular encoded protein. The nucleic acids encoding a Staufen protein or fragment thereof selected from the group consisting of SEQ ID NO: 2, 4, 8 and 10 are distinguished from the proteins themselves by structure and chemistry, the nucleic acids being purine and pyrimidine nucleotides and the proteins being amino acids. The nucleic acids function to encode proteins, that function being determined by their primary nucleotide sequence. The proteins function to bind

ligands in a manner that is specified by their primary amino acid sequence and subsequent secondary and tertiary folding.

Furthermore, searching any of the inventions of groups I and III-VI together would impose a serious and undue search burden. In the instant case, prior art searches of different siRNA sequences, different antisense oligonucleotide sequences, different coding nucleic acid sequences and different polypeptides would not be coextensive. Each search requires different key word searches in divergent patent, non-patent literature and sequence databases. Each search of a different siRNA sequence, different antisense oligonucleotide sequence, different coding nucleic acid sequence and different polypeptide (amino acid) sequence would require different search parameters for each composition in each different sequence database, so as to recover all relevant prior art. Each search would then require subsequent in-depth analysis of the relevant prior art literature and sequence search results, placing an undue and serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform search and examination any of the inventions of groups I and III-VI together.

6. Inventions II and III-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Inventions II and III-VI are outlined above. In the instant case, the inventions are not disclosed as capable of use together and have different modes of operation. Invention

II, as a method of mediating RNA interference, operates based on the siRNA that is required to be administered. Each of inventions III-VI operates to provide a treatment effect based on the structure and chemistry of the required antisense oligonucleotide, protein, chimeric protein or nucleic acid that encodes a protein, respectively, as set forth above in the previous section.

Furthermore, searching any of the inventions of groups I and III-VI together would impose a serious and undue search burden. In the instant case, prior art searches of different methods of administering particular and required siRNAs, and compositions comprising different antisense oligonucleotide sequences, different coding nucleic acid sequences and different polypeptides would not be coextensive. Each search requires different key word searches in divergent patent, non-patent literature and sequence databases. The search for each composition would require a search in each different sequence database that would not be required by the method and a search of the claimed method would require a search for distinctive steps not required by the claimed compositions. Each search would then require subsequent in-depth analysis of the relevant prior art literature and sequence search results, placing an undue and serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform search and examination any of the inventions of groups II and III-VI together.

7. Groups I and III-VI are further restricted as follows:

8. Claims 1, 12, 23, 25 and 28 are each subject to an additional restriction since each is not considered to be a proper genus/Markush. See MPEP 803.02 - PRACTICE RE MARKUSH-TYPE CLAIMS - If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, *unless the subject matter in a claim lacks unity of invention*. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claims 1 and 12 specifically claim siRNAs as listed, that are targeted to and down regulate the expression of Staufen gene by RNA interference. Claim 23 specifically claims antisense sequences as listed, which are targeted to and modulate the expression of Staufen protein. The distinctness of the claimed siRNAs and antisense oligonucleotides is set forth above. However, in regards to the particular siRNAs and antisense claimed, that target particular SEQ ID NO: as claimed, the siRNA and antisense sequences claimed each target and modulate expression of a Staufen

gene, the instant siRNA and antisense sequences are considered to be unrelated, since each siRNA and antisense sequence claimed is structurally and functionally independent and distinct for the following reasons: each siRNA and antisense sequence has a unique nucleotide sequence, each siRNA and antisense sequence targets a different and specific region of a Staufen nucleic acid, and absent evidence to the contrary, each siRNA and antisense sequence, upon binding to a Staufen nucleic acid, is expected to functionally modulate (increase or decrease) the expression of a Staufen nucleic acid, and hence the Staufen protein, to varying degrees. As such the Markush/genus of siRNA and antisense sequences in claims 1, 12 and 23 are not considered to constitute a proper genus, and are therefore subject to restriction.

Claim 23 specifically claims compositions comprising nucleic acids encoding Staufen protein of SEQ ID NO: 2, 4, or 10 or a portion thereof. Each claimed nucleotide sequence (SEQ ID NO:) is considered to be is structurally and functionally independent and distinct because the nucleic acids themselves can differ due to codon degeneracy and because the proteins encoded by each nucleic acid are of different primary amino acid sequence and each nucleic acid sequence does not appear to share a substantial structural feature disclosed as being essential.

Additionally, claim 23 specifically claims compositions comprising Staufen protein or portion thereof having a sequence selected from SEQ ID NO: 1, 3, 5, 6 and 7, claim 25 specifically claims chimeric proteins that comprise a first portion that is a Staufen protein or fragment thereof selected from SEQ ID NO: 2, 4, 8 and 10 and claim 28 specifically claims a vaccine comprising a Staufen protein or fragment thereof selected

from SEQ ID NO: 2, 4, 8 or 10. Each claimed amino acid (SEQ ID NO:) is considered to be is structurally and functionally independent and distinct because each protein is comprised of amino acids that are of different primary amino acid sequence and each protein does not appear to share a substantial structural feature disclosed as being essential.

Furthermore, a search of more than one (1) of the siRNA, antisense, coding nucleic acid or protein sequences as claimed presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the siRNA, antisense, coding nucleic acid or protein sequences. MPEP 808.02 states in part: Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05(C) - 806.05(i), the examiner, in order to establish reasons for insisting upon restriction, must shown by appropriate explanation one of the following:

(C) A different field of search: Where it is necessary to search for one of the distinct subjects in places where no pertinent art to the other subject exists, a different field of search is shown, even though the two are classified together.

It is noted that a search of the available sequence databases produces a listing of references disclosing the sequence most similar to the query sequence. This is the "place" where the examiner searches for prior art. The prior art relating to another query sequence will not be found in this "place"- a different listing of references must be generated and searched by the examiner. Thus a different search is shown, and restriction is proper.

In view of the foregoing, one (1) nucleotide or amino acid sequence as claimed, as it is required by the inventions set forth above that require particular siRNA, antisense, coding nucleic acids or protein sequences, is considered to be a reasonable number of sequences for examination. Accordingly, applicant is required to elect one (1) of the following nucleotide or amino acid sequences, required by the claimed inventions, for examination on the merits in the instant application: one (1) of SEQ ID NO: 1, 3, 5, 6 or 7, an siRNA wherein the sense region comprises SEQ ID NO: 52 or that comprises nucleotides 505-568 of SEQ ID NO: 56 from group I (election of an siRNA wherein the sense region comprises SEQ ID NO: 52 or that comprises nucleotides 505-568 of SEQ ID NO: 56 should include identification of which of SEQ ID NO: 1, 3, 5, 6 or 7 is targeted by the elected siRNA) or one (1) SEQ ID NO: 1, 3, 5, 6, 7 or 10 from group III or one (1) SEQ ID NO: 1, 3, 5, 6, 7 or 10 from group IV or one (1) of SEQ ID NO: 2, 4 8 or 10 from group V or one (1) of SEQ ID NO: 2, 4 8 or 10 from group VI. Note that this is not a species election.

9. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance,

whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file

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